Segmentation of the Brain using Direction-averaged Signal of DWI Images

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ABSTRACT

Segmentation of brain tissue in diffusion MRI image space has some unique advantages. A novel segmentation method using the direction-averaged diffusion weighted imaging (DWI) signal is proposed. Two images can be obtained from the fitting of the direction-averaged DWI signal as a function of b-value: one with superior contrast between the gray matter and white matter; one with prominent CSF contrast. A pseudo T1 weighted image can be constructed and standard segmentation tools can be applied. The method was tested on the HCP dataset using SPM12, and showed good agreement with segmentation using the T1 weighted image with the same resolution. The Dice score was all greater than 0.88 for GM or WM with full DWI data and very stable against subsampling of the DWI data in number of diffusion directions, number of shells, and spatial resolution.

Keywords: Segmentation, diffusion MRI, gray matter, white matter, CSF, direction-averaged

INTRODUCTION

Brain segmentation has great value in medical image analysis as well as clinical applications. Most of the brain segmentation tasks are performed on the T1-weighted (T1w) MR image or in conjunction with a T2-weighted (T2w) image. T1w and T2w images have good contrast between gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). In addition, they usually have high resolution, thus reducing partial volume effects. Nevertheless, segmentation based on other imaging modalities such as diffusion weighted imaging (DWI) has also drawn interest in medical imaging for several reasons. First, it can provide complementary information of tissue contrast. For instance, the GW/WM contrast is not so good in the T1w or T2w images of neonatal brains [1], but is much better in the fractional anisotropy (FA) map derived from the DWI data [2]. Second, DWI segmentation can help with the spatial normalization of diffusion tensor images [3]. Brain segmentation can provide useful information for anatomically-constrained tractography to improve the reliability for fiber tracking [4]. Usually, the segmentation is performed on the T1w image and warped to DWI space. It is well known that DWI images suffer from severe distortion in some areas due to susceptibility artifacts [5], which can introduce errors in the warping of T1w image to the DWI image space. Third, T1w or T2w images suffer from bias field due to the inhomogeneous B1 field and coil sensitivity; the bias field can degrade the segmentation quality because they cannot be separated from the tissue signal readily [6]. Diffusion based segmentation, on the other hand, is less affected by coil sensitivity or B1 field inhomogeneity if the DWI signal is normalized with respect to b0 image. Therefore, segmentation directly on the DWI image is desirable, especially for the diffusion MRI analysis and tractography. Another great value of DWI based segmentation is delineating brain lesions with abnormal diffusion properties in clinical applications [7].

Many methods have been proposed for brain tissue segmentation using DWI images. For instance, Liu et al. used a multi-channel fusion algorithm using FA, mean diffusivity (MD), and tensor information to segment the brain into CSF, GM, and WM [8]. The overlap characterized by the Dice coefficient between the segmentation results in DWI space and that in T1w image space was between 0.6 to 0.7. By using more DTI parametric maps derived from the DWI data, similar results were obtained using a fuzzy C-means algorithm with spatial constraints [9]. The Dice score was 0.89 for WM and 0.93 for GM between their results and the multi-fusion results [8]. However, there was no comparison to the T1w segmentation. Recently, Yap P et al. applied l_0 sparse-group

representation classification on the raw DWI data and achieved a Dice score of ~0.8 for GM and ~0.86 for WM on five subjects when using T1w segmentation as the ground truth [10]. Another method using machine learning achieved an average Dice score of 0.79 by taking the diffusion weighted signal as well as the MD and FA values as features [11].

Because of the complex microstructure that affects the diffusion properties, the classification of brain tissue solely based on DWI derived parametric maps using the tensor model can be challenging. For instance, FA at the voxels with fiber crossing can be similar to the FA in the gray matter. On the other hand, the original DWI signal is too complicated. Even though the DWI signal can be represented by a linear combination of a series of diffusion exemplars for WM, GM, and CSF, these exemplars are not orthogonal and therefore there is still some ambiguity in distinguishing different tissue classes [10]. Hence, it is critical to extract tissue specific microstructure information from the DWI signal.

Recently, it was found that a power law relationship exists between the direction-averaged signal and the diffusion weighting for b-values up to 6000 s/mm^2 [12]. It can be described by this simple equation,

$$log\frac{\bar{S}}{S_0} = \alpha \cdot log\frac{b_1}{b} - \beta, \qquad (1)$$

where $\bar{S}$ is the direction-averaged DWI signal; S_0 is the signal at b = 0; b_1 is the reference b-value; α and β are constants that can be fitted from the signal. In that report, McKinnon et al. also found that α varies with tissue types: $\alpha = 0.56 \pm 0.05$ for white matter and $\alpha = 0.88 \pm 0.11$ for gray matter. The distinct α value between GM and WM makes it a very good index for separating gray matter and white matter. Taking $b = b_1$ in Equation (1), one can easily obtain

$$\beta = -log\frac{\bar{S}_{b_1}}{S_0}, \qquad (2)$$

where $\bar{S}_{b_1}$ is the direction-averaged signal at b_1. If b_1 is large enough (say, b_1 = 1000 s/mm^2), the signal decay for CSF will be significantly larger than that for GM or WM. Hence, β can be used to classify the CSF.

Based on the reasoning above, we propose a simple method to create a T1w-like image for segmentation, to which any segmentation algorithms can be applied. Because α and β indices are

derived from the direction-averaged DWI signal, the segmentation is more microstructure driven and expected to be insensitive to the underlying fiber configuration.

METHODS

Segmentation

The parameters α and β in Equation (1) can be fit from multi-shell DWI data. The key part of the proposed DWI-based segmentation method is generating a pseudo T1w image with good contrast between WM, GM, and CSF. The pipeline is illustrated in Fig. 1 and can be described as follows. First, the α and β parameters are obtained from the DWI data using least square fitting based on Equation (1). The beta image provides excellent contrast for CSF and therefore the CSF can be extracted from it. The histogram of the beta map shows that the GM/WM contributes a big peak with low intensity while the CSF contributes a long tail on the right. A CSF mask (CM) is obtained using a simple threshold. The threshold is chosen to be the value symmetric to 0 on the histogram with respect to the middle line of the peak. Assuming that the GM/WM peak in the histogram is symmetric, i.e., the pure GM/WM voxels will not contribute to any signal higher than the threshold in the beta map, any voxel with β value greater than that threshold is considered as CSF or a mixture of CSF with GM/WM. Then (1 – CM) complementary to CM is a mask for GM/WM. The alpha image is subtracted by a constant to invert the GM/WM contrast. The constant is chosen such that there is adequate separation between GM and background (0 values) in the resultant image. In our case, the constant is set to 2 based on the histograms of the resultant image. Then the resultant image is multiplied by the GM/WM mask to generate a new composite image. The composite image is T1w-like so we call it pseudo T1w image hereafter. The pseudo T1w image can be an input for any brain segmentation algorithm. Here we tried the segmentation tools of SPM12 (Wellcome Centre for Human Neuroimaging, University College London, UK) because sPM is reported to be slightly better than other neuroimaging segmentation tools [13, 14].

We tested our method using the WU-Minn datasets of ten subjects of the Human Connectome Project (HCP) aged 25 – 35 (4 males, 6 females). The data was downloaded from https://db.humanconnectome.org/. The images were acquired on a HCP scanner with 3 T field strength and maximum gradient strength of 300 mT/m. The DWI acquisition parameters are: TR/TE = 5520/89.5 ms; flip angle = 78°; bandwidth = 1488 Hz/pixel; multiband factor = 3. Each dataset has 288 preprocessed DWI images with isotropic resolution of 1.25 mm and b-value of

[1000, 2000, 3000] s/mm^2. The preprocessing included motion and eddy current correction. The dataset also contains a T1-weighted image that was transformed from the original high-resolution T1-weighted image to the DWI image space and resampled to the same resolution as the DWI image.

We applied the proposed method to obtain the pseudo T1w images and exported it to SPM12 to do the segmentation. The T1-weighted image was also processed in SPM12 for segmentation and the result served as a ground truth in evaluating our method. The segmentation of the pseudo T1w image was compared with the T1 based segmentation using the Dice similarity coefficient, defined as the ratio of the overlap to the mean of the two images. To further assess the goodness of our method, the T1w image was also segmented using FSL (FMRIB, Oxford University, UK) and the Dice score between FSL and SPM12 was computed as a reference on three subjects. Since both FSL and SPM12 output probabilistic maps for three classes of GM/WM/CSF, a threshold of 0.5 for each class was used when computing the Dice scores.

Segmentation on sub-sampled DWI data

To test the method on DWI data with degraded quality, we also performed segmentation using only a subset of the HCP DWI data: one was using only the lowest two shells (b = 1000 s/mm^2, and b = 2000 s/mm^2), the other was using 1/3 of the DWI data by down-sampling the number of directions. The results were compared with segmentation results of T1-weighted image using SPM12 as well.

On three subjects, we further generated low-resolution data by combining signals from a cubic of 8 voxels. The resultant DWI data has an isotropic resolution of 2.5 mm, close to those acquired from clinical settings. The segmentation on the low-resolution DWI data was compared with that derived from high resolution T1w image but re-sampled in the same way.

DWI analysis

The DWI data was processed in FSL to compute the brain mask from the b0 image using the BET tool and to compute the mean diffusivity map using the FDT tool. All the comparisons for segmentation were conducted within the brain mask. In addition, the (neurite orientation dispersion and density imaging) NODDI analysis was performed using the NODDI Matlab toolbox developed by UCL Microstructure Imaging Group (http://mig.cs.ucl.ac.uk/index.php). The neurite

density map was obtained for each subject. The correlation between neurite density and α values was computed.

Simulation

To investigate the relationship between α and intrinsic microstructure of brain tissue, we generated the synthetic diffusion signals using analytic formulation of multi-compartment models similar to the method that is used in Camino [15, 16]. A simple simulation was performed using a one-fiber cylinder-zeppelin model for 100 voxels with a uniform distribution of the diameter of cylinder between 0 – 2 μm. No CSF component was considered. The fraction of intra-cellular volume (f) was set to 0.2, 0.4, 0.6, and 0.8, respectively. The parallel diffusivity D_{intra} was set to 2250 $\mu m^2/s$; which characterize the intrinsic diffusivity inside the cylinders and along the principal direction of the zeppelins. We used b-value = [1000, 2000, 3000, 4000, 5000, 6000] s/mm^2, and the same b-vectors as used in the HCP protocol for each shell. The time between the two pulses, Δ = 43.1 ms and the pulse duration, δ = 10.6 ms were also identical to those in the HCP data. Gaussian noise was added to the signal such that the SNR of the signal for the b0 image was set to 20. The simulation resulted in 90 directions per shell and 18 b0 images for each voxel.

Data and code availability statement

The data used in this work is the HCP data, which is publicly available. The code was written in Matlab (MathWorks, Natick, MA, USA) and can be shared upon request. A python version of the method has been implemented in DIPY (https://dipy.org/) and will be available once the paper is published.

RESULTS

Fig. 2 shows the alpha and beta images for three HCP subjects. All alpha images show good GM/WM contrasts; all beta images show good CSF components.

Fig. 3 shows the images of α, and β, the pseudo T1w image, and the T1w image. The alpha image showed a good contrast between GM and WM. However, some WM areas have low signal that are similar to the CSF, as depicted by the blue ellipse. The beta image does not have much GM/WM contrast, but shows a distinct CSF component, making it very useful in extracting the

CSF. The pseudo T1w image looks like the T1-weighted image. The T1-weighted image has good GM/WM contrast but it is hard to distinguish CSF from GM in some regions.

Fig. 4 compares the results of segmentation in SPM12 using the pseudo T1w image and T1w image. The segmentation from the pseudo T1w image is overlaid by the segmentation using the T1w image. The two approaches match very well for segmentations of GM and WM, and CSF in ventricles. There is some mismatch at the edge but not on any large continuous anatomy.

The Dice scores between different methods are listed in Table 1 and Table 2. The agreement between T1w image and pseudo T1w image on segmentation is all above 0.88 for GM and WM. These agreements are very close to those between SPM12 and FSL (Table 1 (d) columns). The Dice score for CSF is slightly lower, which is mainly influenced by much fewer voxels in CSF. There is a very slight decrease of Dice score if less data is used for segmentation. However, there is no compelling evidence of showing which way is better between reducing number of shells and reducing number of directions. The Dice scores on low-resolution DWI data are listed in Table 3 for three subjects. The results show that even with a lower resolution of 2.5 mm, which is typically feasible in a clinical setting, the proposed method yields similar segmentation results as the T1w image. An example of the segmentation images is shown in supplementary material.

The simulation results are displayed in Fig. 5 in which the direction-averaged diffusion MRI signals are plotted as a function of b-value. The average α values obtained from the linear fitting according to Equation (1) are α = [0.975, 0.766, 0.652, 0.548] for f = [0.2, 0.4, 0.6, 0.8], clearly shows a negative correlation between α and f. The negative correlation also holds for *in vivo* data. Fig. 6 shows a map of neurite density calculated from NODDI (in NODDI model, the neurite density is characterized by the intra-cellular volume faction, f_{icv}, which is equivalent to f in our simulation) for one slice of subject 1 along with the corresponding alpha image. The contrast between GM and WM in the neurite density map is opposite to the contrast in the alpha image. The negative correlation between neurite density and the α metric for WM voxels is clearly demonstrated from the scatter plot. The correlation coefficient is -0.94.

DISCUSSION

We have developed a novel method of classifying the three types of brain tissue based on the direction-averaged signal of the DWI images. A pseudo-T1w image can be constructed for

segmentation. One advantage of this approach is that no bias field needs to be estimated. The performance is very good even without using any advanced segmentation tools. The Dice score with respect to the segmentation based on T1w image is mostly above 0.9 for both GM and WM on three HCP subjects. The Dice score is not only much higher than those reported in previous studies [8-11], but are also very close to that between SPM12 and FSL in our study and reported scores between various popular brain segmentation tools [14]. While it is difficult to judge our method without knowing the ground truth for segmentation, we are confident that our method produces comparable segmentation results as using T1w images. The pseudo T1w image purely generated from diffusion data provides an alternative mechanism for segmenting the brain into GM, WM, and CSF. Moreover, the Dice scores remain the same using DWI data with fewer shells or directions, suggesting that this method can work well on state-of-the-art DWI data that typically has more than two shells and 60 directions such as the ABCD protocol. It is a robust method that is easy to implement and is well suited for providing guidance for fiber tracking.

The β value characterizes the signal decay from b=0 to b=1000 s/mm^2, as explicitly written in Equation (2). The beta image is similar to the MD map calculated from the b=1000 s/mm^2 shell. If including all three shells in MD calculation, the CSF value will be significantly underestimated (see supplementary material) because of the noise floor for CSF and invalidity of tensor model at high b-values, and the difference between CSF and GM/WM in the MD map is not big enough to separate them. Unlike the fitting of α from multiple b-values, the computation of β only needs one diffusion shell like b=1000 s/mm^2 so that the beta image can be obtained in clinical settings. Because the GM/WM signal is suppressed, it might be valuable in some clinical applications, e.g., in detecting edema.

The α value of 0.5 at high b-value in the white matter can be well explained by the "stick" model of the intracellular component [17, 18]. Our simulation using a one-fiber cylinder-zeppelin model shows that the α value decreases while f increases in the b-value range of 1000 – 6000 s/mm^2. Here the cylinder models the intra-axonal compartment and the extra-axonal compartment is modeled by the zeppelin. Because f represents the contribution of the intra-axonal component, our result indicates that the extra-axonal component with fraction (1-f) shifts α toward higher values. This observation is in line with the simulation results by Veraart et al. In real tissue, the intra-axonal fraction f is related to the neurite density in the white matter. Hence, one can deduce

that α is negatively correlated to the neurite density in the white matter. By applying the NODDI model on the HCP data, a high correlation of -0.94 between neurite density and α value was observed in the white matter. As pointed by Lampinen et al., NODDI may be able to capture the relative variation of axonal density in the white matter [19]. Therefore, it is plausible that neurite density plays an important role in determining alpha value in the white matter. However, whether the difference in neurite density between GM and WM contributes substantially to the contrast observed in the alpha image is unknown. There is a discussion about why the α value of gray matter deviates from 0.5 by Mckinnon et al. [12]. They hypothesize that the water permeability for the cell membranes of neurites is higher for gray matter, which is partially supported by a study suggesting that neurites are in notable exchange with another compartment in the gray matter [20]. Nevertheless, other factors such as diffusion diffusivity might play a role in distinguishing GM from WM as well. Using a second-order approximation, the direction-averaged signal is solely determined by the b-value and the axial and longitudinal diffusivity of the axonal segment, which consists of the axon and its typical surrounding volume (extracellular volume associated with that axon) [21]. Although the power law relationship in equation (1) cannot be deduced from their model, the density plot of the per-axon diffusion coefficients clearly shows clusters of GM, WM, CSF, and partial volume effects. Therefore, the concept of per-axon diffusion coefficients provides a different angle to look at the difference between GM and WM.

The thresholding of β value in our method ensures that the CSF mask does not contain any GM or WM although the voxels within the GM/WM mask might have partial volume effect with CSF. Hence, with smaller CSF contamination, our method produces better segmentation for GM and WM on the pseudo T1w image, as confirmed by much higher Dice scores. However, the segmentation of CSF is not optimal using hard thresholding. As CSF is mostly adjacent to GM, a small threshold of beta can lead to more inclusion of GM in CSF classification. It is possible to develop multi-channel segmentation methods using alpha and beta images simultaneously. That will be our future research. In addition, we have not tested this method to pathological conditions, which is an area to explore in the future.

In summary, a new segmentation method is proposed for multi-shell DWI data based on characteristics of signal change with b-values. The method was tested on the HCP dataset using SPM and FSL, and showed good agreement with segmentation using the T1-weighted image with

the same resolution. The method also works well with DWI data with fewer shells and gradient directions, or lower resolution.

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Table 1. Dice scores between segmentation results of the proposed method and SPM12 on three HCP subjects using (a) full data; (b) 2 shells; (c) 1/3 data, 3 shells. The Dice score between segmentation results of SPM12 and FSL on the T1w image is also listed as references (d).

	Subj1 (119732)				**Subj2 (120111)**				**Subj3 (120515)**			
	(a)	(b)	(c)	(d)	(a)	(b)	(c)	(d)	(a)	(b)	(c)	(d)
WM	.92	.90	.90	.92	0.91	.93	.91	0.91	.89	.88	.88	.90
GM	.91	.90	.90	.92	0.92	.92	.91	0.91	.89	.89	.89	.92
CSF	.77	.77	.76	.86	0.77	.78	.78	0.83	.76	.76	.76	.86

Table 2. Dice scores between segmentation results of the proposed method and SPM12 of the other seven subjects using (a) full data; (b) 2 shells; (c) 1/3 data, 3 shells.

HCP ID	**WM**			**GM**			**CSF**		
	(a)	(b)	(c)	(a)	(b)	(c)	(a)	(b)	(d)
100408	.92	.91	.91	.89	.89	.89	.81	.81	.81
101915	.90	.89	.89	.90	.89	.89	.76	.76	.76
103515	.91	.90	.90	.90	.89	.89	.82	.82	.82
105216	.90	.89	.89	.89	.88	.88	.80	.80	.79
110411	.92	.91	.91	.89	.89	.88	.80	.80	.80
112819	.90	.89	.89	.90	.89	.89	.79	.79	.78
118225	.91	.90	.90	.89	.88	.88	.79	.79	.77

Table 3. Dice scores between segmentation results of the proposed method on low-resolution DWI data (2.5 mm isotropic) and SPM12 on high resolution T1w image re-sampled to the same resolution for three HCP subjects.

	Subj1 (119732)		**Subj2 (120111)**		**Subj3 (120515)**	
	High res	Low res	High res	Low res	High res	Low res
WM	0.92	0.89	0.91	0.88	0.89	0.92
GM	0.91	0.92	0.92	0.91	0.89	0.82
CSF	0.77	0.73	0.77	0.75	0.76	0.81

Figure Captions

Fig. 1. Flow chart of creating a pseudo T1w image from DWI with good contrast between GM, WM, and CSF for segmentation.

Fig. 2. Alpha and beta maps of a representative slice for 3 HCP subjects.

Fig. 3. Images derived from the DWI data (alpha, beta, and the pseudo T1w image) show different contrasts between the gray matter, white matter, and CSF. As a comparison, a T1w image with the same resolution is shown at the right. The blue ellipse indicates CSF-like low intensity in some white matter area in the alpha map; there is little contrast between GM and WM for the beta map.

Fig. 4. Comparison of the segmentation results from SPM12 using the pseudo T1w image and T1w image. The segmentation from the pseudo T1w image (black and white) is overlaid by the segmentation using the T1w image (red). The overlap of the two segmentations is shown pink in the figure. The threshold of the probabilistic map is set to 0.5.

Fig. 5. Simulation of direction-averaged diffusion MRI signal as a function of b-value using a one-fiber cylinder-zeppelin model. The fraction of intra-cellular volume (f) is varied from 0.2 to 0.8. The highest b-value is 6000 s/mm^2 and the reference b-value b_1 is 1000 s/mm^2.

Fig. 6. A comparison between neurite density map computed from NODDI model (top left) and alpha image (top right) on one slice of subject 1. The negative correlation between these two images can be clearly seen from the scatter plot (bottom). The correlation coefficient is -0.87.